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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,170	10/22/2001	Yongchang Qiu	GII5412AUSA	4670

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EXAMINER

WALLENHORST, MAUREEN

ART UNIT	PAPER NUMBER
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1743

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/045,170

Applicant(s)

QIU ET AL.

Examiner

Maureen M. Wallenhorst

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-23 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ 6) ☐ Other: ____

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1. Claims 1-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

On lines 3 and 7 of claim 1, the phrase "the disulfide bonds" lacks antecedent basis, and should be changed to --disulfide bonds--. Part d) of claim 1 is indefinite and vague since it is not understood why the disulfide bonds in the digested peptides have to be reduced when they were already reduced in part a) of the method. It is not understood why two steps of disulfide bond reduction are recited in the method. Part g) of claim 1 is indefinite since it recites eluting the cysteine-containing peptides. However, it is not clear what the peptides are being eluted from, i.e. some type of separation column, etc?

On line 4 of claim 2, the phrase "cysteine-containing labels" lacks antecedent basis, and should be changed to --cysteine-containing peptides--. On line 5 of claim 2, it is suggested to insert the phrase --of claim 1--after the phrase "in the reacting step (e)" so as to provide further clarification. On line 6 of claim 2, the phrase "form the reagent" should be changed to --form of the reagent--so as to make proper sense.

On line 2 of claim 3, the phrase "is selected" should be changed to --selected--so as to make proper sense.

On lines 1-2 of claim 16, the phrase "which is selected from the group consisting of" should be deleted and replaced by the phrase --which comprises--since claim 16 only recites a single compound, not a list of multiple compounds.

Claim 22 is indefinite since it is not clear whether the set of cysteine-tagging reagents all have the same structure as the compound recited in claim 16.

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2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 16-19 and 21-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds recited in claim 20, does not reasonably provide enablement for all possible compounds having a thiol-specific reactive group attached to a non-biological polymer via a linker. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification only provides support for the thiol-specific reactive group being maleimide, haloacetyl, or one of the conjugated double bond structures listed on page 7 of the specification. In addition, the specification only lists certain ones of non-biological polymers being included in the recited compound listed on page 4 of the specification, not all possible non-biological polymers imaginable. Specifically, the specification only provides enablement for a very small proportion of the compounds encompassed by claims 16-19 and 21-23, in particular, the compounds recited in instant claim 20 since it is only these compounds that are synthesized and used in the method of protein analysis in the examples given in the specification.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Huang et al.

Huang et al teach of a polyethylene glycol (PEG) copolymer for carrying and releasing cysteine-containing peptides. The PEG copolymer is attached to a thiol-specific reactive group via a linker. The thiol-reactive group is cysteamine-thiopyridine, and the linker is a carbonyl group (C=O). See reaction schemes 1 and 2 on page 613 of Huang et al. The thiopyridine attachment sites on the PEG copolymer allow for binding to cysteine-containing peptides.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claims 1-4, 14-19 and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aebersold et al (WO 00/11208, submitted in the Information Disclosure Statement filed on January 18, 2002) in view of Huang et al. For a teaching of Huang et al, see previous paragraphs in this Office action.

Aebersold et al teach of a method for the quantitative analysis of proteins in mixtures. The method involves the use of affinity-labeled protein reactive reagents that allow for the selective isolation of peptide fragments. The isolated peptide fragments are characterized by mass spectrometric techniques. The method comprises the steps of reducing the disulfide bonds of proteins in a sample to produce free thiol (SH) groups, digesting the proteins with trypsin to form peptides, and reacting the peptides with an affinity-labeled protein reactive reagent. The affinity label is preferably biotin, which is attached to a thiol-specific reactive group via a linker. The thiol-specific reactive group can be a haloacetyl group or a maleimide. The linker may comprise acidic or basic groups such as COOH groups. The reagent can be isotopically labeled by substitution of the linker atoms with stable isotopes (i.e. deuterium). In the method, one sample of peptides is combined with a labeled form of the reagent (i.e. isotopically heavy form), and a second sample is combined with an unlabeled form of the reagent (i.e. isotopically light form). Aliquots of the samples labeled with the isotopically different reagents (i.e. heavy and light reagents) are then combined. Excess affinity tagged reagent is then washed away, and the tagged peptides are run through a separation column containing a capture reagent for the tagged peptides (i.e. avidin agarose). The bound peptides are then eluted, and analyzed using a mass-spectrometry based method. Aebersold et al also teach of a kit for the analysis of proteins by mass spectrometry, which comprises the affinity-labeled protein reactive reagent, one or more

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proteolytic enzymes for the digestion of proteins in a sample, and a set of substantially chemically identical differentially labeled affinity tagged reagents. See claims 42-48 in Aebersold et al. Aebersold et al fail to teach that the affinity-labeled protein reactive reagent can contain a thiol-reactive group attached to a non-biological polymer via a linker.

Based upon the combination of Aebersold et al and Huang et al, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to replace the affinity-labeled protein reactive reagent taught by Aebersold et al with the PEG copolymer taught by Huang et al since Aebersold et al teach that the affinity labeled protein reactive reagents bind to cysteine-containing peptides through a thiol-specific reactive group, and the PEG copolymer taught by Huang et al also contains a thiol-specific reactive group therein bound to the PEG copolymer via a linker that is able to bind to cysteine-containing peptides.

10. Claims 5-13 and 20 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims since none of the prior art of record teaches or fairly suggests the specific structure of the compounds recited in these claims containing a thiol-reactive group bound to a linker, which is in turn bound to an acid-labile group, which is in turn bound to a non-biological polymer such as polystyrene or polyethylene glycol.

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Please make note of: Shen and Shadle et al who teach of polymers bound to a thiol-reactive group, such as maleimide, that bind to cysteine-containing peptides.

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12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maureen M. Wallenhorst whose telephone number is 571-272-1266. The examiner can normally be reached on Monday-Wednesday from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden, can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0661.

Maureen M. Wallenhorst
Primary Examiner
Art Unit 1743

mmw

January 24, 2004

Maureen M. Wallenhorst
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GROUP 1000 1700